

We claim:

1. An isolated siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA (SEQ ID NO: 1), or an alternative splice form, mutant or cognate thereof.

2. The siRNA of claim 1, wherein the cognate of the human ICAM-1 mRNA sequence is mouse ICAM-1 mRNA (SEQ ID NO: 2).

3. The siRNA of claim 1, wherein the sense RNA strand comprises one RNA molecule, and the antisense RNA strand comprises one RNA molecule.

4. The siRNA of claim 1, wherein the sense and antisense RNA strands forming the RNA duplex are covalently linked by a single-stranded hairpin.

5. The siRNA of claim 1, wherein the siRNA further comprises non-nucleotide material.

6. The siRNA of claim 1, wherein the siRNA further comprises an addition, deletion, substitution or alteration of one or more nucleotides.

7. The siRNA of claim 1, wherein the sense and antisense RNA strands are stabilized against nuclease degradation.

8. The siRNA of claim 1, further comprising a 3' overhang.

9. The siRNA of claim 8, wherein the 3' overhang comprises from 1 to about 6 nucleotides.

10. The siRNA of claim 8, wherein the 3' overhang comprises about 2 nucleotides.
11. The siRNA of claim 3 wherein the sense RNA strand comprises a first 3' overhang, and the antisense RNA strand comprises a second 3' overhang.
12. The siRNA of claim 11, wherein the first and second 3' overhangs separately comprise from 1 to about 6 nucleotides.
13. The siRNA of claim 12, wherein the first 3' overhang comprises a dinucleotide and the second 3' overhang comprises a dinucleotide.
14. The siRNA of claim 13, where the dinucleotide comprising the first and second 3' overhangs is dithymidylic acid (TT) or diuridylic acid (uu).
15. The siRNA of claim 8, wherein the 3' overhang is stabilized against nuclease degradation.
16. A retinal endothelial cell comprising the siRNA of claim 1.
17. A recombinant plasmid comprising nucleic acid sequences for expressing an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof.

18. The recombinant plasmid of claim 17, wherein the nucleic acid sequences for expressing the siRNA comprise an inducible or regulatable promoter.

19. The recombinant plasmid of claim 17, wherein the nucleic acid sequences for expressing the siRNA comprise a sense RNA strand coding sequence in operable connection with a polyT termination sequence under the control of a human U6 RNA promoter, and an antisense RNA strand coding sequence in operable connection with a polyT termination sequence under the control of a human U6 RNA promoter.

20. The recombinant plasmid of claim 17, wherein the plasmid comprises a CMV promoter.

21. A recombinant viral vector comprising nucleic acid sequences for expressing an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof.

22. The recombinant viral vector of claim 21, wherein the nucleic acid sequences for expressing the siRNA comprise an inducible or regulatable promoter.

23. The recombinant viral vector of claim 21, wherein the nucleic acid sequences for expressing the siRNA comprise a sense RNA strand coding sequence in operable connection with a polyT termination sequence under the control of a human U6 RNA promoter, and an antisense RNA strand coding sequence in operable connection with a polyT termination sequence under the control of a human U6 RNA promoter.

24. The recombinant viral vector of claim 21, wherein the recombinant viral vector is selected from the group consisting of an adenoviral vector, an adeno-associated viral vector, a lentiviral vector, a retroviral vector, and a herpes virus vector.

25. The recombinant viral vector of claim 21, wherein the recombinant viral vector is pseudotyped with surface proteins from vesicular stomatitis virus, rabies virus, Ebola virus, or Mokola virus.

26. The recombinant viral vector of claim 24, wherein the recombinant viral vector comprises an adeno-associated viral vector.

27. A pharmaceutical composition comprising an siRNA and a pharmaceutically acceptable carrier, wherein the siRNA comprises a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof.

28. The pharmaceutical composition of claim 27, further comprising lipofectin, lipofectamine, cellfectin, polycations, or liposomes.

29. A pharmaceutical composition comprising the plasmid of claim 17, or a physiologically acceptable salt thereof, and a pharmaceutically acceptable carrier.

30. The pharmaceutical composition of claim 29, further comprising lipofectin, lipofectamine, cellfectin, polycations, or liposomes.

31. A pharmaceutical composition comprising the viral vector of claim 21 and a pharmaceutically acceptable carrier.

32. A method of inhibiting expression of human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof, comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof, such that the human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof, is degraded.

33. The method of claim 32, wherein the subject is a human being.

34. The method of claim 32, wherein expression of human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof is inhibited in one or both eyes of the subject.

35. The method of claim 32, wherein expression of human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof is inhibited in retinal pigment epithelial cells of the subject.

36. The method of claim 32, wherein the effective amount of the siRNA is from about 1 nM to about 100 nM.

37. The method of claim 32, wherein the siRNA is administered in conjunction with a delivery reagent.

38. The method of claim 37, wherein the delivery agent is selected from the group consisting of lipofectin, lipofectamine, cellfectin, polycations, and liposomes.

39. The method of claim 38, wherein the delivery agent is a liposome.

40. The method claim 39, wherein the liposome comprises a ligand which targets the liposome to cells expressing ICAM-1.

41. The method of claim 40, wherein the ligand binds to receptors on endothelial, epithelial, fibroblastic, hematopoietic or tumor cells.

42. The method of claim 41, wherein the endothelial cells are retinal vascular epithelial cells.

43. The method of claim 41, wherein the hematopoietic cells are selected from the group consisting of tissue macrophages, mitogen-stimulated T lymphocyte blasts, germinal center dendritic cells in tonsils, germinal center dendritic cells in lymph nodes, and germinal center dendritic cells in Peyer's patches.

44. The method of claim 41, wherein the ligand comprises a monoclonal antibody.

45. The method of claim 39, wherein the liposome is modified with an opsonization-inhibition moiety.

46. The method of claim 45, wherein the opsonization-inhibiting moiety comprises a PEG, PPG, or derivatives thereof.

47. The method of claim 32, wherein the siRNA is expressed from a recombinant plasmid.

48. The method of claim 32, wherein the siRNA is expressed from a recombinant viral vector.

49. The method of claim 48, wherein the recombinant viral vector comprises an adenoviral vector, an adeno-associated viral vector, a lentiviral vector, or a herpes virus vector.

50. The method of claim 49, wherein the recombinant viral vector is a lentiviral vector which is pseudotyped with surface proteins from vesicular stomatitis virus, rabies virus, Ebola virus, or Mokola virus.

51. The method of claim 32, wherein the siRNA is administered by an enteral administration route.

52. The method of claim 51, wherein the enteral administration route is selected from the group consisting of oral, rectal, and intranasal.

53. The method of claim 32, wherein the siRNA is administered by a parenteral administration route.

54. The method of claim 53, wherein the parenteral administration route is selected from the group consisting of intravascular administration, peri- and intra-tissue administration, subcutaneous injection or deposition, subcutaneous infusion, intraocular administration, and direct application at or near the site of neovascularization.

55. The method of claim 54, wherein the intravascular administration is selected from the group consisting of intravenous bolus injection, intravenous infusion, intra-arterial bolus injection, intra-arterial infusion and catheter instillation into the vasculature.

56. The method of claim 54, wherein the peri- and intra-tissue injection is selected from the group consisting of peri-tumoral injection, intra-tumoral injection, intra-retinal injection, and subretinal injection.

57. The method of claim 54, wherein the intraocular administration comprises intravitreal, intraretinal, subretinal, subtenon, peri- and retro-orbital, trans-corneal or trans-scleral administration.

58. The method of claim 54, wherein the direct application at or near the site of neovascularization comprises application by catheter, corneal pellet, eye dropper, suppository, an implant comprising a porous material, an implant comprising a non-porous material, or an implant comprising a gelatinous material.

59. The method of claim 58, wherein the site of neovascularization is in the eye, and the direct application at or near the site of neovascularization comprises application by eyedropper.

60. A method of inhibiting cell adhesion or cell adhesion-mediated pathologies in a subject, comprising administering to a subject an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof.

61. The method of claim 60, wherein the cell adhesion or cell adhesion-mediated pathologies are selected from the group consisting of AIDS-related dementia, allergic conjunctivitis, allergic rhinitis, Alzheimer's disease, angiogenesis, antigen presentation, asthma, atherosclerosis, toxic nephritis, immune-based nephritis, contact dermal hypersensitivity, corneal/limbic injury, type I diabetes, complications arising from type I diabetes, Graves' disease, inflammatory bowel disease, inflammatory lung diseases, inflammatory sequelae of viral infections, inflammatory skin disorders, allograft rejection, immune cell interactions such as T-cell killing, mixed lymphocyte reaction, T-cell mediated B-cell differentiation, meningitis, multiple sclerosis, multiple myeloma, myocarditis, pulmonary fibrosis, reperfusion injury, restenosis, retinitis, rheumatoid arthritis, septic arthritis, stroke, tumor metastasis, and uveitis.



62. The method of claim 61, wherein the inflammatory skin disease is allergic contact dermatitis, fixed drug eruption, lichen planus, or psoriasis.

63. The method of claim 61, wherein the allograft is a renal, liver or bone marrow transplant.

64. The method of claim 62, wherein the angiogenesis is non-pathogenic and is associated with production of fatty tissues, cholesterol production, or endometrial neovascularization.

65. A method of treating an angiogenic disease in a subject, comprising administering to a subject in need of such treatment an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof, such that angiogenesis associated with the angiogenic disease is inhibited.

66. The method of claim 65, wherein the angiogenic disease comprises a cancer.

67. The method of claim 66, wherein the cancer is selected from the group consisting of breast cancer, lung cancer, head and neck cancer, brain cancer, abdominal cancer, colon cancer, colorectal cancer, esophagus cancer, gastrointestinal cancer, glioma, liver cancer, tongue cancer, neuroblastoma, osteosarcoma, ovarian cancer, pancreatic cancer, prostate cancer, retinoblastoma, Wilm's tumor, multiple myeloma, skin cancer, lymphoma, and blood cancer.

68. The method of claim 65, wherein the angiogenic disease is selected from the group consisting of diabetic retinopathy and age-related macular degeneration.

69. The method of claim 68, wherein the angiogenic disease is age-related macular degeneration.

70. The method of claim 65, wherein the siRNA is administered in combination with a pharmaceutical agent for treating the angiogenic disease, which pharmaceutical agent is different from the siRNA.

71. The method of claim 70, wherein the angiogenic disease is cancer, and the pharmaceutical agent comprises a chemotherapeutic agent.

72. The method of claim 70, wherein the chemotherapeutic agent is selected from the group consisting of cisplatin, carboplatin, cyclophosphamide, 5-fluorouracil, adriamycin, daunorubicin, and tamoxifen.

73. The method of claim 65, wherein the siRNA is administered to a subject in combination with another therapeutic method designed to treat the angiogenic disease.

74. The method of claim 73, wherein the angiogenic disease is cancer, and the siRNA is administered in combination with radiation therapy, chemotherapy or surgery.

75. A method of treating complications arising from type I diabetes in a subject, comprising administering to a subject in need of such treatment an effective amount of an siRNA comprising a sense RNA strand and an antisense RNA strand, wherein the sense and an antisense RNA strands form an RNA duplex, and wherein the sense RNA strand comprises a nucleotide sequence substantially identical to a target sequence of about 19 to about 25 contiguous nucleotides in human ICAM-1 mRNA, or an alternative splice form, mutant or cognate thereof.

76. The method of claim 75, wherein the complications arising from type I diabetes are selected from the group consisting of diabetic retinopathy, diabetic neuropathy, diabetic nephropathy and macrovascular disease.

77. The method of claim 76, wherein the macrovascular disease is coronary artery disease, cerebrovascular disease or peripheral vascular disease.